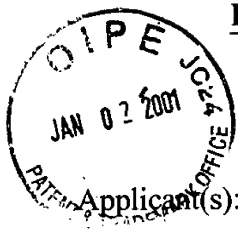


GAU 1044/p

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**



**Patent Examining Operations**



**27162**

PATENT TRADEMARK OFFICE

Applicant(s): Mosca, et al.

Serial No: 09/267,456

Filed: March 12, 1999

Title: Mesenchymal Stem Cells as Immunosuppressants

Attorney

Docket No.: 640100-295

Art Unit: 1644

Examiner: Ewoldt

**RECEIVED**

JAN 10 2001

Customer No. 27162

**TRANSMITTAL LETTER**

TECH CENTER 1600/2900

Assistant Commissioner for Patents  
Washington, D.C. 20231

SIR:

Enclosed please find the following:

1. Response to Office Action dated July 5, 2000;
2. Request for three months Extension of Time;
3. Check No. 3803 in the amount of \$445.00; and
4. A self-addressed, postage paid, return receipt postcard, date stamp and return of which is respectfully requested.

The Commissioner is authorized to charge payment of any additional filing fees required under 37 C.F.R. 1.16 associated with this communication or credit any overpayment to Deposit Account No. 03-0678.

**FIRST CLASS CERTIFICATE**

I hereby certify that this correspondence is being deposited today with the U.S. Postal Service as First Class Mail in an envelope addressed to:

Assistant Commissioner for Patents  
Washington, D.C. 20231

*Raymond J. Lillie* 12/27/2000  
Raymond J. Lillie, Esq. Date

Respectfully submitted,

Raymond J. Lillie, Esq.

Reg. No. 31,778

CARELLA, BYRNE, BAIN, GILFILLAN,  
CECCHI, STEWART & OLSTEIN

Six Becker Farm Road  
Roseland, New Jersey 07068

T: (973) 994-1700

F: (973) 994-1744

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Examining Operations

#10  
1/11/01  
RECEIVED

JAN 10 2001

TECH CENTER 1600/2900

Applicant(s): Mosca, et al.

Serial No: 09/267,456

Art Unit: 1644

Filed: March 12, 1999

Examiner: Ewoldt

Title: Mesenchymal Stem Cells as Immunosuppressants

Attorney

Docket No.: 640100-295

Assistant Commissioner of Patents  
Washington, D.C. 20231

SIR:

In response to the Office Action dated July 5, 2000, reconsideration of the above-identified application is hereby respectfully requested.

Claims 1-4 stand rejected under 35 U.S.C. 103 as being unpatentable over Robinson '320 in view of Gerson, et al. '625.

Claims 1-4 stand rejected under Bloom, et al. '299 in view of Gerson, et al. '625.

These rejections are respectfully traversed.

The present invention, in one aspect as defined in Claim 1, is directed to a method of inhibiting a T-cell response to an antigen. The method comprises contacting T-cells with mesenchymal stem cells modified to present the antigen, thereby inhibiting a T-cell response to the antigen.

In another aspect of the present invention, as defined in Claim 2, a T-cell response to an antigen is inhibited by administering to a host human mesenchymal stem cells that have been modified to present the antigen, thereby inhibiting a T-cell response to the antigen.

The cited references do not disclose or even remotely suggest to one of ordinary skill in the art the modification of mesenchymal stem cells to present an antigen in order to inhibit a T-cell response to an antigen.

Robinson describes the genetic engineering of cells with genes encoding HLA Class I and HLA Class II molecules, along with a gene encoding an antigen. Such cells may be used to suppress an unwanted immune response to the antigen. The cells which may be genetically engineered may be activated T-cells, fibroblasts, eosinophils, keratinocytes, astrocytes, microglial cells, thymic cortical epithelial cells, endothelial cells, Schwann cells, retinal pigment epithelial cells, myoblasts, vascular smooth muscle cells, chondrocytes, enterocytes, thyrocytes, and kidney tubule cells. Robinson, however, does not disclose or even remotely suggest to one of ordinary skill in the art that any type of stem cells, including mesenchymal stem cells as claimed by Applicants, may be modified in order to present an antigen in order that such cells may be employed to inhibit a T-cell response to an antigen. Robinson, therefore, does not even remotely suggest Applicants' claimed methods to one of ordinary skill in the art, and thus does not render Applicants' claimed methods obvious to one of ordinary skill in the art.

Bloom discloses inducing an anergic and unresponsive state in T-lymphocytes by presentation of an antigen by a cell other than a normal antigen presenting cell. The cell other than a normal antigen presenting cell is transfected with a polynucleotide encoding a major histocompatibility complex antigen.

Bloom, like Robinson, does not disclose or even remotely suggest to one of ordinary skill in the art that stem cells, including mesenchymal stem cells, can be modified to present an antigen in order to inhibit a T-cell response to the antigen. Bloom, therefore, also does not render Applicants' claimed methods obvious to one of ordinary skill in the art.

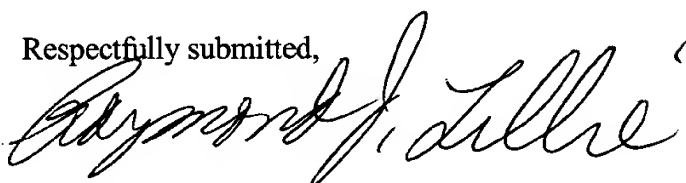
Gerson discloses the genetic engineering of mesenchymal stem cells such that the mesenchymal stem cells express physiologically active or pharmacologically active proteins. The cells could express the proteins *in vitro*, or they could be employed in gene therapy. The proteins may be hormones, matrix proteins, cytokines, adhesion molecules, detoxification enzymes, and proteins employed in tissue repair.

Gerson, however, does not disclose or even remotely suggest to one of ordinary skill in the art that the mesenchymal stem cells can be modified such that they present an antigen to T-cells, whereby the modified mesenchymal stem cells inhibit a T-cell response to the antigen.

Applicants discovered that mesenchymal stem cells, when provided with an antigen, exhibit an inhibitory effect on T-cell stimulation, as opposed to an enhancement of T-cell stimulation. The cited references, taken alone or in combination, do not disclose or even remotely suggest to one of ordinary skill in the art that one can provide mesenchymal stem cells with an antigen, and use such modified mesenchymal stem cells to inhibit a T-cell response against the antigen. At best, the cited prior art renders it obvious to try Applicants' claimed method. Such a standard for obviousness within the meaning of 35 U.S.C. 103, however, is improper. (See Uniroyal, Inc. v. Rudkin-Wiley Corp., 5 U.S.P.Q.2d 1434 (C.A.F.C. 1988), at 1440; In Re Dow Chemical, 5 U.S.P.Q.2d 1529 (C.A.F.C. 1988), at 1531; American Hospital Supply Corp. v. Travenol Laboratories, Inc., 223 U.S.P.Q. 577 (C.A.F.C. 1984), at 582.) Therefore, the cited references do not render Applicants' methods as claimed obvious to one of ordinary skill in the art.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections under 35 U.S.C. 103 be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Raymond J. Lillie". The signature is fluid and cursive, with the first name being the most prominent.

Raymond J. Lillie, Esq.  
Registration No. 31,778